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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,933	08/13/2001	Pierre Leroy	032751-066	6916

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EXAMINER	
PRIEBE, SCOTT DAVID	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,933	LEROY ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Jul. 23 & Sep 24, 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-42,44,46,47,51-58 and 60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42,44,46,47,51-58 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 42, 44, 57, 58, and 60 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action of 4/23/04. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive. With respect to claims 42 and 60, Applicant points to Example 6 and Figure 11 as additional support for these claims. However, these parts of the specification describe the same species described on pages 13, 18, and in original claim 28, which is the only disclosed species readable on these claims. Applicant then points to original claim 27, which is directed specifically to the fusion of extracellular domains I and II of CD4 with the constant γ_3 region of the heavy chain of the 2F5 antibody, and working backwards through a series of improper multiple dependent claims, then down through other dependent claims as support for their being a generic toxic protein fused to the fusion protein of original claim 27. However, there is no more clear support for these claims by this convoluted route than there is in the specification itself. Applicant is turning the claims inside-out in order to justify their argument. It remains that

there is no explicit indication that Applicant had contemplated fusing a generic toxic substance to a generic antibody fused to the CD4 domains. There is only one disclosed species that is readable on these claims, from N- to C- terminus, the extracellular I and II domains of CD4, constant γ_3 region of the 2F5 antibody, and human angiogenin. The description of a generic antibody being fused to the CD4 extracellular domains, such as on page 8, makes clear that the antibody retains its ability to the antigen to which it was directed, i.e. the fusion protein is bifunctional. In contrast, the antigen binding regions of the 2F5 antibody are absent in the fusion proteins or original claims 27 and 28, i.e. in these cases the constant region of the 2F5 antibody is used simply as a scaffold to which the CD4 extracellular domains are attached, i.e. the fusion protein is not bifunctional. Consequently, it is unclear how the description of this single species would have suggested to one of skill in the art that Applicant had contemplated the genus of claims 42 and 60, where the antibody could be any antibody directed to an epitope of a pathogen (or fragment of the antibody), and the toxic substance could be any toxic substance fused specifically to the C-terminus of the generic antibody.

Applicant argues that *Purdue Pharma* is not relevant here because the fact situation is different because the instant specification generally described fusing toxic proteins or immunopotentiating proteins to antibodies. However, what the specification did not generally teach was attaching specifically the CD4 extracellular domains to any antibody and any toxic substance. *Purdue Pharma* at 1486-1487 makes clear that in general picking one specific characteristic among others from a species and using it as the basis for a generic claim is the type of overreaching that the written description requirement was designed to guard against. As to the meaning of "or," the issue in *Brown* was whether "or" actually meant "and", not whether "or"

also meant "and," as Applicant is arguing here. In *Kustom Signals*, the issue was whether "either ... or" could mean "and." However, the court in *Brown* pointed out that "or" could be exclusive, i.e. "either ... or," or it could be inclusive, i.e. "... or ... or both," and that one must look to the specification to decide whether it is exclusive or inclusive. As indicated in the original grounds of rejection and above, there is no general description that supports "or" being inclusive with respect to an antibody or part thereof to which is fused both a toxic substance and an immunopotentiating substance. There is only one species described where both an immunopotentiating and toxic substance are fused to all or part of an antibody. All three components of the fusion protein are defined. Unlike other embodiments where only one type of substance is fused to the antibody, the part of the antibody in the species no longer comprises its antigen binding regions. The discussion of this single species does not suggest or imply that one extend this three component fusion to a general concept.

With respect to claims 44, 57 and 58, Applicant explains that the protein of interest, comprises a heavy and light chain of an antibody, is modified at the N-terminus, but not that both the heavy and light chains be modified. However, this explanation does not make sense. A monomeric protein consists of a single polypeptide. A multimeric protein comprises two or more polypeptides, which are referred to as protein chains in the specification. While a polypeptide or protein chain has an N-terminus, a multimeric protein comprises multiple polypeptides, each with their own N-terminus. There is no N-terminus of a multimeric protein, there are N-termini of the polypeptides that make up the protein. Consequently, the claim leaves open which and how many of the heavy and light chains are modified at their N-terminus. This is not supported by the original specification.

Applicant refers to page 4, line 35 to page 7, line 29, as describing antibodies to be used in the inventions. However, the specification is directed to more than is being claimed. The specification describes proteins of interest that are simply multimeric, i.e. they need not be antibodies at all. Page 4, line 35 to page 7, line 29, of the specification describes subject matter where the protein of interest is an antibody that is not modified by peptide sequences that are exogenous to antibodies, such as a toxic substance or immunopotentiating substance. Further modification of antibodies is described beginning on page 7, line 30. The specification at page 10 describes fusing the exogenous peptide sequence to one chain, not to a multimeric protein. Fusion of the coding sequence of the peptide downstream of coding sequence for an antibody heavy chain would fuse the peptide to the C-terminus of the heavy chain. This part of the specification supports the rejection, i.e. that the specification does not describe fusing the CD4 domains to the multimeric protein at its N-terminus. Page 13, lines 21-27, describe fusing CD4 extracellular domains specifically to part of a heavy chain hinge region of the 2F5 antibody (also see page 18, Example 6, original claims 27 and 28, and Fig. 11). Such a polypeptide would be expected to form a homodimer. Also, this region of the antibody lacks the region which would bind the 2F5 light chains, so it would not form a heterotetramer as claimed, were the light chain also expressed in the same cell.

Claim Rejections - 35 USC § 103

Claims 40, 41, 44, 46, 47, and 51-58 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Allaway et al. (WO 94/19017) in view of Berkner (WO 90/01550) for the reasons of record set forth in the Office action of 4/23/04.

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive. Claims 40 and 44 have been amended to replace "directed against" with "capable of recognizing." However, these are two ways of saying basically the same thing. Applicant argues that the interpretation of the claim language in the rejection is unreasonable, in that the claim requires that the part of the antibody be at least the part that recognizes the epitope, and that such interpretation is consistent with the specification. However, it is noted that the features upon which applicant relies (i.e., that the part of the antibody be the part that recognizes the epitope) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the only species described in the specification (page 13, lines 21-28; Example 6; original claims 27 and 28; and Fig. 11) that comprises the CD4 extracellular domains consists of, in order, the extracellular domains of CD4 fused to the constant γ_3 region of the heavy chain of the 2F5 antibody (and optionally, human angiogenin fused to the C-terminus of the constant γ_3 region). This region of the antibody does not contain the epitope binding region (i.e. the variable region). Consequently, the interpretation of the claims indicated in the rejection is consistent with the specification, i.e. that the "part" of the antibody can be any part. At the extreme, the part could be a single amino acid present in an antibody.

Conclusion

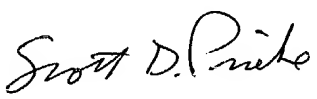
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Scott D. Priebe
Primary Examiner
Art Unit 1632